SCIENCE CAPSULES

Eating Fish Reduces Risk of Stroke. For a long time, researchers have suspected that the amount of fish in a person's diet affects the likelihood of experiencing a stroke. Some studies indicate that diets high in fish and omega-3 polyunsaturated fatty acids, found primarily in fish and animals that feed on fish, reduce a person's risk for thrombotic strokes (strokes caused by blood clots), but others indicate that a similar diet can increase the risk for hemorrhagic strokes (strokes caused by bleeding in the brain). New data from the Nurses' Health Study have revealed that women who ate fish 2-4 times per week had half the incidence of thrombotic stroke and the same risk of hemorrhagic stroke as women with similar cardiovascular risk factors who ate fish less than once a month. Thus, consuming several servings of fish each week may constitute a safe and easy way for women to reduce their likelihood of suffering a stroke.

Iso H, Rexrode KM, Stampfer MJ, Manson JE, Colditz GA, Speier FE, Hennekens CH, and Willett WC: Intake of fish and omega-3 fatty acids and risk of stroke in women. The Journal of the American Medical Association 285: 304-312, 2001.

DASH Hypertension Diet Also Lowers Cholesterol. Researchers recently announced that individuals with high blood cholesterol can benefit significantly from adopting an eating plan originally designed to prevent and treat high blood pressure, adding one more tool to the armament of interventions known to decrease coronary heart disease risk. The DASH (Dietary Approaches to Stop Hypertension) diet is low in saturated and total fat and cholesterol, and high in fruits, vegetables, and low fat-dairy foods. In addition to lowering blood pressure in hypertensive patients and reducing elevated levels of the amino acid homocystine (a risk factor for heart disease, stroke, and peripheral vascular disease), the DASH diet significantly reduces levels of total cholesterol and low-density lipoprotein (LDL), or "bad" cholesterol.

Obarzanek E, Sacks FM, Vollmer WM, Bray GA, Miller ER III, Lin PH, Karanja NM, Most-Windhauser MM, Moore TJ, Swain JF, Bales CW, and Proschan MA, on behalf of the DASH Research Group: Effects on blood lipids of a blood pressure–lowering diet: the dietary approaches to stop hypertension (DASH) trial. American Journal of Clinical Nutrition 74: 80-89, 2001.

Reducing Sodium Leads to Substantial Drop in Blood Pressure. Adopting the DASH (Dietary Approaches to Stop Hypertension) diet – a food plan that is rich in fruits, vegetables, and dairy products and low in saturated fat, total fat, and cholesterol – is an established method of lowering high blood pressure. Now, researchers have found that reducing sodium consumption also lowers blood pressure, whether a person has high blood pressure or normal blood pressure, and whether he or she follows the DASH diet or eats a typical U.S. diet. However, combining the DASH diet with a limitation of 1500 mg of sodium per day showed the most dramatic results, lowering the blood pressures of people with hypertension to levels similar to those achievable by a single drug. These results illustrate how dietary modifications, along with other lifestyle changes, could help prevent the rise of blood pressure with age and allow individuals to control their hypertension with fewer drugs or even none at all.

Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER III, Simons-Morton DG, Karanja N, and Lin PH: Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. The New England Journal of Medicine 334: 3-10, 2001.

Weight Loss Reduces Risk of Sleep Apnea. Sleep apnea is a prevalent and potentially serious medical condition characterized by repeated episodes of airway obstruction during sleep and excessive daytime sleepiness. Investigators studying nearly 700 adults found that weight gains of 5 to 20 percent increase the risk of developing sleep apnea by 2.5- to 37-fold, respectively. More importantly, weight loss was associated with reduced severity of sleep apnea and decreased likelihood of developing moderate to severe sleep apnea. These results strongly suggest that weight loss and prevention of weight gain, through diet or exercise, are effective strategies for managing or preventing sleep apnea.

Peppard PE, Young T, Palta M, Dempsey J, and Skatrud J: Longitudinal study of moderate weight change and sleep-disordered breathing. The Journal of the American Medical Association 284: 3015-3021, 2000.

Raloxifene Does Not Affect Cognitive Function in Postmenopausal Women. Estrogen replacement therapy (ERT) is used to treat menopausal symptoms and reduce the risk of osteoporosis and heart disease. ERT may also have a beneficial effect on cognition, but increases the risk of breast or uterine cancer in some women. Raloxifene is a selective estrogen receptor modulator (SERM) used for the prevention and treatment of osteoporosis that is not associated with an increased risk of breast or uterine cancer. Raloxifene had not been tested for either positive or negative effects on cognitive function. Results from the Multiple Outcomes of Raloxifene Evaluation (MORE) trial indicated no significant differences between the treatment groups and controls in performance on cognitive tests or the development of dementia after three years, although there was a slightly lower risk of cognitive decline in verbal memory and attention with raloxifene treatment. Women who choose raloxifene treatment for osteoporosis can be reassured that it does not have negative effects on cognitive function.

Yaffe K, Krueger K, Sarkar S, Grady D, Barrett-Connor E, Cox DA, and Nickelsen T: Cognitive function in postmenopausal women treated with raloxifene. The New England Journal of Medicine 344: 1207-1213, 2001.

Positive Emotions in Early Life Linked to Longevity. Findings from the Nun Study indicate that positive emotional content in early life autobiographies was strongly associated with longevity six decades later. Nuns who expressed more positive emotions in their autobiographies lived significantly longer than nuns expressing fewer positive emotions. Finding such a strong association between written positive emotional expression and longevity indicates a need for research that sheds light on the underlying mechanisms responsible for and associated with this relationship.

Danner DD, Snowden DA, and Friesen WV: Positive emotions in early life and longevity: findings from the nun study. Journal of Personality and Social Psychology 80: 804-813, 2001.

Depression and Agitation in Alzheimer's Disease: Effects on Caregivers. Previous research has examined the factors contributing to stress and depression in caregivers of an AD family member. This study found that at the beginning of the caregiver's participation in the study, the greater the level of depression in the care recipient, the greater the level of depression in the caregiver. Wives of male AD victims and caregivers in poor health themselves were at particular risk for depression. This study demonstrates that the well being of the caregiver and care recipient are closely related. This finding suggests that in order to develop appropriate interventions, research examining sustained quality of life and physical and mental well being of both the care recipient and the caregiver is needed. The findings also support interventions for caregivers early in the family member's illness.

Neundorfer MM, McClendon MJ, Smyth KA, Stuckey JC, Strauss ME, and Patterson MB: A longitudinal study of the relationship between levels of depression among persons with Alzheimer's disease and levels of depression among their family caregivers. Journals of Gerontology (in press 2001).

Alzheimer's Disease Transgenic Model Immunization: Non-Toxic Peptide Vaccine. The accumulation of amyloid plaques is a defining characteristic of Alzheimer's disease (AD). These plaques are formed in the brain from amyloid beta (A_), a peptide fragment of amyloid precursor protein (APP). In 1999, researchers showed that long-term vaccination with A_ peptides caused reductions in the deposition of amyloid in APP transgenic mice. There is a concern, however, about the use of aggregated A_ in vaccinations because A_ can be toxic and could also be a "seed" for still more A_ fibril formation. Transgenic mice were immunized for seven months with a synthetic peptide similar to A_, but which is not toxic and does not form amyloid fibrils. The synthetic peptide reduced the amount of amyloid by approximately 85 percent in regions of brain most affected in AD. Importantly, the levels of soluble A_ peptide, which may be the toxic form, were reduced by close to 60 percent. Inflammation, assessed by the presence or absence of a particular type of central nervous system cell – the microglia – was also reduced. The study shows that a vaccine using a non-toxic peptide modeled on the A_ peptide can be effective and would pose a lower risk of serious side effects. Such an approach may prove to be an effective therapy for reducing amyloid burden or preventing amyloid deposition in AD.

Sigurdsson EM, Scholtzova H, Mehta PD, Frangione B, and Wisniewski T: Immunization with a nontoxic/ nonfibrillar amyloid-Beta homolgous peptide reduces Alzheimer's disease-associated pathology in transgenic mice. American Journal of Pathology 159: 439-447, 2001.

Molecular Basis of Alpha Virus Assembly. Two groups of viruses with different genomic organization have been found to have similar surface or shell structures, suggesting a common ancestor and a common mechanism for infecting mammalian hosts. The alphaviruses cause illnesses such as encephalitis and arthritis while the flaviviruses cause the dengue, West Nile, and yellow fevers. Together they cause more than half of the insect-borne diseases in humans and animals world-wide. Understanding the structure of the viral shell and the mechanism for

fusing with mammalian hosts will guide the design of inhibitors to prevent viral entry and infection.

Pletnev SV, Zhang W, Mukhopadhyay S, Fisher BR, Hernandez R, Brown DT, Baker TS, Rossmann MG, and Kuhn RJ: Locations of carbohydrate sites on alphavirus glycoproteins show that E1 forms an icosahedral scaffold. Cell 105: 127-36, 2001.

Quicker Cancer Assays Possible with Genetically Altered Mice. New genetically engineered mouse models offer the possibility of assessing environmental compounds for cancer-causing properties both more quickly and with fewer animals. Our ability to use these substitutes, however, depends upon them being identical to normal mice in how they break down, or metabolize, environmental agents. In this study, two genetically altered mouse strains, Tg.AC and p53+/- mice, were exposed to well-characterized chemicals. Upon examining the metabolic pathways and critical enzyme production of these mice, these researchers concluded that the ability of these mice to metabolize chemicals is not compromised by the altered genomes.

Sanders JM, Burka,LT, Chanas B, and Matthews, HB: Comparative xenobiotic metabolism between Tg.AC and p53+/- genetically altered mice and their respective wild types. Toxicological Sciences 61: 54-61, 2001.

Important Insight into Food Poisoning. *Salmonella* is one of several bacteria that can cause food poisoning. Understanding how it works at the cellular and molecular levels can give insight into how to treat it. The body normally disposes of bacteria by employing specialized cells, the phagocytes, to consume and digest bacteria found in the body. *Salmonella* has the ability to trick normal intestinal cells to acquire certain characteristics of phagocytes, so they accumulate the bacteria, but in a non-destructive manner. This paper shows that *Salmonella* has the ability to hijack the cellular machinery via the enzyme inositol polyphosphatase, allowing for specific changes in cell architecture that precede phagocytosis.

Zhou D, Chen LM, Hernandez L, Shears SB and Galán JE: A Salmonella inositol polyphosphatase acts in conjunction with other bacterial effectors to promote host-cell actin cytoskeleton rearrangements and bacterial internalization. Molecular Microbiology 39: 248-259, 2001.

Environmental Agent Inhibits Testosterone Production. Compounds that cause a marked increase in the size and number of peroxisomes (small organelles found in high concentrations in liver cells, whose main function is detoxifying chemicals such as therapeutic drugs and environmental agents) are known as peroxisome proliferators. In addition to their effects on the liver, these compounds induce changes in the testis. Perfluorodecanoic acid (PFDA), an industrial chemical, has been reported to cause anatomical disturbances to the testis and specifically to a particular type of testicular cell called the Leydig cell. Leydig cells in the testis produce testosterone, which is necessary for normal sexual function and fertility. Researchers have found that a receptor known as the peripheral-type benzodiazepine receptor (PBR) is the target of PFDA. PBR acts as a transport mechanism for cholesterol, a precursor of testosterone.

A decreased number of functioning receptors causes decreased testosterone production, which results in the inhibition of sperm production and reduced fertility.

Boujrad N, Vidic B, Gazouli M, Culty M, and Papadopoulos V: The peroxisome proliferator perfluorodecanoic acid inhibits the peripheral-type benzodiazepine receptor (PBR) expression and hormone-stimulated mitochondrial cholesterol transport and steroid formation in Leydig cells. Endocrinology 141: 3137-3148, 2000.

Risky Health Practices in Adult Men Traced to Their Experiences as Children. An NIH-funded study examined whether men who reported a history of unwanted sexual activity during childhood (USC) engaged in more high-risk sexual behaviors and reported increased problems with substance abuse than men not reporting USC. The study was based on interview data from the NIH Multisite HIV Prevention Trial, a national study that enrolled predominantly African-American and Hispanic/Latino men and women at high risk for HIV/STD infection recruited from sexually transmitted disease clinics and health service organizations in seven regional sites throughout the U.S. Study data from baseline interviews of almost 2,700 men ages 18-70 revealed that those with a history of USC are much more likely to engage in high-risk sexual practices and have elevated rates of alcohol and illicit drug use. This research suggests that routine health screening of adults and children should address the possibility of past or present child abuse, and has implications for developing HIV prevention and counseling programs for those at greatest risk.

The NIMH HIV/STD Prevention Trial Group: unwanted sexual activity during childhood and risk behaviors among men at high risk for HIV infection. American Journal of Public Health (in press 2001).

How Does Depression Contribute to Mortality in Older Adults? Depression can result from medical illness and disability, but a growing literature suggests it can also influence biological changes linked to medical morbidity and mortality, particularly from heart disease, the Nation's leading cause of death. In a study of more than 5,000 people over age 65, researchers found that individuals with high levels of depressive symptoms were 25 percent more likely to die within 6 years than those who had low levels of depressive symptoms, after controlling for a large number of socio-demographic, disease, and biological and behavioral risk factors. To explain the phenomenon, the investigators proposed a model that suggests some older adults become trapped in a downward spiral in which behavior, medical illness, and depression mutually influence one another to undermine individual biological integrity. Possible mechanisms linking depression and mortality include behavioral risk factors such as inactivity, increased alcohol consumption, eating and sleeping problems, and poor adherence to treatment for medical problems. Potential biological risk factors related to depression include activation of the hypothalamic-pituitary-adrenal (HPA) axis and compromised immune function, which may in turn predispose individuals to infectious disease, cancer, or the exacerbation of existing medical illness. An important clinical implication of the model is the use of multiple intervention approaches to treat the depression, the behavioral problems, the medical illness and its functional consequences, or some combination of these behavioral and biological factors. A better

understanding of these mechanisms can guide future attempts to modify them and potentially reduce the morbidity and premature mortality among older people with depression.

Schulz R, Beach SR, Ives DG, Martire LM, Ariyo AA, and Kop WJ: Association between depression and mortality in older adults. Archives of Internal Medicine 160: 1761-1768, 2000.

Schulz R, Martire LM, Beach SR, and Scheier MF: Depression and mortality in the elderly. Current Directions in Psychological Science 9(6): 204-208, 2000.

Perceived Stigma Can Affect Treatment Adherence for Depressed Older Adults. As part of a treatment research study, younger and older depressed adults rated the degree to which they felt stigmatized by virtue of their mental disorder. Younger depressed adults rated higher stigma than older individuals. Yet, older adults who perceived high stigma were more likely to discontinue antidepressant treatment than older adults with lower perceived stigma. Overall, stigma may play an important role in treatment adherence.

Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Raue P, Friedman SJ, and Meyers BS: Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. American Journal of Psychiatry 58(3): 479-481, 2001.

Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Friedman SJ, and Meyers BS: Perceived stigma and patient-rated illness severity as predictors of adherence to antidepressant drug treatment. Psychiatric Services (in press 2001).

Keys to Successful Aging: Results of a 60-Year Prospective Study. Using the most recent assessments from the Harvard Study of Adult Development, ongoing now for 60+ years, investigators classified predictor variables for a successful old age that had been assessed in subjects before age 50 as either "uncontrollable" factors (e.g., parental social class, family cohesion, major depression, ancestral longevity, childhood temperament and physical health) and "controllable" factors (alcohol abuse, smoking, marital stability, exercise, body mass index, and coping mechanisms). Among the "uncontrollable" variables, only having a depressive disorder before age 50 was an independent predictor of group status. However, each of the six "controllable" variables emerged as predictive of whether the now 65- to 80-year-old men would be categorized as "Happy-Well" or "Sad-Sick." Among college men with fewer than four protective factors (such as stable marriage, good exercise habits, absence of alcohol abuse) before age 50, more than three-quarters were among the Sad-Sick or were prematurely dead. By contrast, more than half of both college and inner-city men with 5 or 6 protective factors before age 50 were in the Happy-Well group. The data from this well-characterized cohort demonstrate that maintaining mental and physical health with aging depends heavily upon behavioral and psychosocial factors, and healthy behaviors across the life span.

Vaillant GE, and Mukamal K: Successful aging. American Journal of Psychiatry 158(6): 839, 2001.

Isolation of a Potential Vaccine Candidate Against *Leishmania*. The leishmaniases are a group of diseases with a broad range of clinical manifestations caused by various species of parasites of the genus *Leishmania*. These diseases, which affect many millions of people worldwide, are transmitted by various species of the sandfly. From earlier studies, scientists had determined that proteins in the saliva of the sandfly increase the efficiency of transmission of the *Leishmania* parasite. Recently, NIH scientists characterized several of the salivary gland proteins and demonstrated that a vaccine containing one of these proteins can protect mice from *Leishmania* infection. These results suggest that the sandfly salivary gland proteins may serve as viable candidates for a vaccine against *Leishmania*.

Valenzuela JG, Belkaid Y, Garfield MK, Mendez S, Kamhawi S, Rowton ED, Sacks DL, and Ribeiro JMC: Toward a defined anti-*Leishmania* vaccine targeting vector antigens: characterization of a protective salivary protein. Journal of Experimental Medicine 194: 331-342, 2001.

Improved TB Vaccine Provides Enhanced Protection. Tuberculosis (TB) has a devastating impact globally, with 8 million new cases and 2 million deaths each year. The current vaccine, bacillus Calmette-Guérin (BCG), provides some protection against tuberculosis, mainly in children, but its efficacy in adults is limited. In response to the need for a more potent vaccine against TB, NIH-supported researchers constructed a candidate BCG vaccine that produces a *Mycobacterium tuberculosis* protein, the 30-kDa major secretory protein. Guinea pigs vaccinated with the modified BCG were protected better against TB than animals vaccinated with the unmodified BCG. This demonstrates that the existing vaccine against tuberculosis, BCG, can be improved by bioengineering, and this approach may lead to new candidate vaccines for humans.

Horwitz MA, Harth G, Dillon BJ, and Masleša-Gali_ S: Recombinant bacillus Calmette-Guérin (BCG) vaccines expressing the *Mycobacterium tuberculosis* 30-kDa major secretory protein induce greater protective immunity against tuberculosis than conventional BCG vaccines in a highly susceptible animal model. Proceedings of the National Academy of Sciences USA 97: 13853-13858, 2000.

Families Can Provide a Shield Against a Child's Initial Drug Use. To investigate how various risk factors and resiliency factors interact with gender and ethnicity to impact substance use, researchers surveyed 609 students in the southwest U.S. The risk factors studied were: family stress, unsafe neighborhoods, and parental substance use. The resiliency factors included: good family relations, a family that is not permissive, and high religiosity. The researchers found that a *lack* of resiliency factors were highly predictive of past month substance use, having received a drug offer, and acceptance of the offer. Both risk and resiliency factors affected age of initiation and the lifetime number of drug offers, with low resiliency Mexican-American females, African-American males, and European-American males receiving the most drug offers. Not surprisingly, those with low resiliency and high risk were likely to have started using drugs at earlier ages. Among males, risk factors were directly connected with substance use, and the effect of resiliency factors was mediated by age of first use, whereas for females resiliency factors played a much greater role. These results suggest that for maximum effect substance use

prevention efforts should focus on building resiliency prior to first drug use, particularly for males.

Moon DG, Jackson KM, and Hecht ML: Family risk and resiliency factors, substance use, and the drug resistance process in adolescence. Journal of Drug Education 30(4): 373-398, 2000.

Drug Users in Communities with Low HIV Rates More Likely to Engage in High-risk Behaviors. Researchers compared HIV-related risk behaviors among more than 12,000 intravenous drug users (IDUs) in 22 communities with various HIV seroprevalence (percent of people who test positive for HIV) rates. The researchers found that drug users living in low seroprevalence (5 percent or less) communities were more likely to engage in risky injection and sex-related behaviors than those living in communities with higher rates of HIV infection (moderate: 6 to19 percent, or high: 20 percent or more). IDUs living in sites with lower seroprevalence rates had the highest rates of having sex with another IDU during the past 30 days, and reported the highest level, 85 percent, of unprotected sexual acts. Rates of injection were about 2.5 times higher in high seroprevalence communities than in the low or moderate communities, yet more than 50 percent of drug users in low seroprevalence communities reported using syringes belonging to other people compared to the other sites. These findings highlight the importance of employing prevention methods in all communities, not just those with the highest rates of HIV infection, as drug use is now the major risk factor identified in new cases of AIDS in the U.S.

Deren S, Beardsley M, Coyle S, Singer M, and Kang SY: HIV risk behaviors among injection drug users in low, medium, and high seroprevalence communities. AIDS and Behavior, 2001.

Being Overweight at Age 13 Predicts Insulin Resistance at Age 22. In this study, measurements (including body mass index, waist circumference, insulin and cholesterol levels) were made in children at age 13 and again at age 22. The children who were overweight at age 13 were more likely at age 22 to be overweight, have increased insulin resistance, and higher levels of total and LDL cholesterol, which increases the risk of heart disease. Strategies to manage excess weight gain during childhood may modify the level of cardiovascular risk factors in young adulthood.

Steinberger J, Moran A, Hong CP, Jacobs DRJ, and Sinaiko AR: Adiposity in childhood predicts obesity and insulin resistance in young adulthood. Journal of Pediatrics 138: 469-473, 2001.

Dental Plaque Formation: Pellicle Protein Characterization. After eruption and exposure to the mouth, tooth surfaces are immediately coated by an organic film, resulting from the selective adsorption of specific proteins from oral fluids. This poorly characterized film, known as the acquired enamel pellicle, provides a surface to which bacteria adhere during the initial stages of dental plaque formation. In this study, pellicle was collected from twelve individuals and the proteins analyzed by a combination of analytical techniques. Eleven major pellicle proteins were

identified. A detailed understanding of the composition and structure of the pellicle might lead to the development of interventions that could reduce or modify bacterial colonization on tooth surfaces.

Yao Y, Grogan J, Zehnder M, Lendenmann U, Nam B, Wu Z, Costello CE, and Oppenheim FG: Compositional analysis of human acquired enamel pellicle by mass spectrometry. Archives of Oral Biology 46: 293-303, 2001.

Increased Risk for Bone and Liver Cancers in Nuclear Plant Workers. Exposure to radiation has been associated with increased risk for certain cancers. In a study of approximately 11,000 persons who worked in the Mayak nuclear plant in Russia between 1948 and 1958, NIH scientists demonstrated for the first time that exposures to plutonium resulted in excess risk of bone and liver cancer when workers with a high versus a low body burden of plutonium were compared. The analysis also showed that the risk of each type of cancer increased with increasing body burden of plutonium. The workers in this study were exposed to both internally deposited plutonium and external gamma radiation at much higher levels than those allowed today.

Gilbert ES, Koshurnikova NA, Sokolnikov M, Khokhryakov VF, Miller S, Preston DL, Romanov SA, Shilnikova NS, Soslova KG, and Vostrotin VV: Liver cancers in Mayak workers. Radiation Research 154: 246-252, 2000

Koshurnikova NA, Gilbert ES, Sokolnikov M, Khokhryakov VF, Miller S, Preston DL, Romanov SA, Shilnikova NS, Soslova KG, and Vostrotin VV: Bone cancers in Mayak workers. Radiation Research 154: 237-245, 2000.

Cancer Risk in DES-exposed Mothers. Diethylstilbestrol (DES) is a synthetic form of estrogen that was given to some pregnant women between 1938 and 1971 to reduce their risk of miscarriage. Past studies have shown that women who took DES have an increased risk of breast cancer; a recent study confirmed these results. However, the researchers also found that breast cancer risk is not further increased in former DES users who also have a family history of breast cancer, or in women who used oral contraceptives or hormone replacement therapy. This research also found no increased risk of ovarian, endometrial (uterine), or other cancer.

Hartge P, Hatch EE, Hoover RN, Titus-Ernstoff L, Greenberg ER, Palmer J, Ricker W, Kaufman R, Noller K, Herbst AL, and Colton T: Cancer risk among women given DES during pregnancy. British Journal of Cancer 84: 126-133, 2001.

Hereditary Retinoblastoma and Lung Cancer Risk. Retinoblastoma is a rare malignant tumor of the retina that predominantly affects children under 5 years old. The disease can be hereditary (inherited) or nonhereditary. Most cases of retinoblastoma are caused by the absence of, or a mutation in, the RB1 gene, which normally suppresses tumor development. Children with the inherited form of retinoblastoma have an increased chance of developing other types of cancers, especially later in life. A study of 1,604 persons who had survived retinoblastoma found an excess of early-onset lung cancers in this group. The findings suggest that carriers of RB1

mutations may be highly susceptible to smoking-induced lung cancers and are candidates for aggressive smoking cessation efforts.

Kleinerman RA, Tarone RE, Abramson DH, Seddon JM, Li FP, and Tucker MA: Hereditary retinoblastoma and lung cancer risk. Journal of the National Cancer Institute 92: 2037-2039, 2001.

Genetics and Nicotine Addiction. Individual differences in propensity to nicotine dependence appear to be mediated, in part, by genetic factors. In a recent study, in people with a certain combination of serotonin transporter genes (termed the 5-HTTLPR S genotype), neuroticism (an anxious, tense, or touchy personality) was associated with nicotine dependence, smoking to improve mood, and smoking for stimulation. In people with a different combination of these genes (the 5-HTTLPR L genotype), neuroticism and nicotine dependence were not associated. Assessment of HTTLPR genotype (L or S) and neuroticism could help identify smokers who might be more responsive to different types of smoking-cessation treatment.

Lerman C, Caporaso NE, Audrain J, Main D, Boyd NR, and Shields PG: Interacting effects of the serotonin transporter gene and neuroticism in smoking practices and nicotine dependence. Molecular Psychiatry 5(2): 189-192, 2000.

New Cytotoxins for Tumor Cells. Several cytotoxic proteins derived from bacterial protein toxins are in therapeutic use as anti-tumor agents. However, a recurrent problem is their nonspecific toxicity for normal cells. Because of their high inherent potency, even a small amount of these cytotoxins can seriously damage normal cells in the vicinity. NIH researchers have now modified anthrax toxin proteins so that they only attack tumor cells that express an enzyme called plasminogen activator. This enzyme is overproduced in a significant number of malignant human tumors of the head and neck, colon, breast, ovaries, lung, bladder, thyroid, liver, pancreas, skin, and blood. The ability of this new cytotoxin to selectively kill tumor cells in mixed cultures of normal and tumor cells in laboratory studies suggests that it may have the potential to target tumors in humans. Animal studies will help determine whether the cytotoxin is effective in preventing cancer invasion and metastasis.

Liu S, Bugge TH, and Leppla SH: Targeting of tumor cells by cell surface urokinase plasminogen activator-dependent anthrax toxin. The Journal of Biological Chemistry 276: 17976-17984, 2001.

Long-term Estrogen Replacement Therapy Reduces the Risk of Cataracts. Cataracts are a major cause of visual impairment and blindness. Cataract surgery is one of the most frequently performed surgical procedures in the U.S. Researchers have found that postmenopausal women on estrogen replacement therapy are less likely to develop cataracts. Women and their doctors should take this potential benefit into consideration when discussing whether or not estrogen replacement therapy is appropriate for them.

Worzala K, Hiller R, Sperduto RD, Mutalik K, Murabito JM, Moskowitz M, D'Agnostino RB, and Wilson PWF: Postmenopausal estrogen use, type of menopause, and lens opacities: The Framingham Studies. Archives of Internal Medicine 161: 1448-1454, 2001.

Vaginal Delivery After a Cesarean Section. Approximately 60 percent of women with a prior delivery by cesarean section opt to attempt labor and vaginal delivery in a subsequent pregnancy. Compared to the risk of rupture during a repeat cesarean section, the risk during uninduced labor was over 3 times as great, while the risk during labor induced by prostaglandins increased to 15 times as great. Women attempting vaginal delivery after a cesarean section need to be aware of these potential risks, and the decision to perform an initial cesarean delivery should include the potential effect on future pregnancies.

Lydon-Rochelle M, Holt VL, Easterling TR, and Martin DP: Risk of uterine rupture during labor among women with a prior cesarean delivery. The New England Journal of Medicine 345: 3-8, 2001

Depression Intervention in College-age Women. Negative thinking and low self-esteem are risk factors for developing depression among college-age women. Depression impairs academic performance, school satisfaction, and social performance. Researchers tested a preventive cognitive-behavioral intervention program for college-age women who had been screened and found to have a degree of depression. The intervention consisted of six carefully structured weekly group sessions. Women in the intervention group showed fewer depressive symptoms, less negative thinking, and higher self-esteem even at an 18-month follow-up.

Peden AR, Rayens MK, Hall LA, and Beebe LH: Preventing depression in high-risk college women: a report of an 18-month follow-up. Journal of American College Health 49: 299-306, 2001.

Exercise Can Safely Help HIV+ Patients Maintain Weight and Endurance. Researchers conducted an exercise intervention with HIV+ adults. Study subjects completed a 12 week directed exercise program. Afterward, the test subjects showed greater endurance on a treadmill test, along with a decrease in weight, body mass index, and abdominal girth, with no difference noted in CD4+ cell counts. Aerobic exercise among HIV+ patients can safely manage adverse physical signs and symptoms such as fatigue and reduced aerobic capacity.

Smith BA, Neidig JL, Nickel JT, Mitchell GL, Para MF, and Fass RJ: Aerobic exercise: effects on parameters related to fatigue, dyspnea, weight and body composition in HIV-infected adults. AIDS 15: 693-701, 2001.

Managing Cardiovascular Risk Factors During Encounters for Coronary Bypass Surgery. Investigators examined the status of risk factor control for chronic cardiovascular disease patients who were admitted for coronary bypass surgery. Almost half of all patients were overweight, and most had diets high in total fat and saturated fat. Only one-third exercised regularly. No patients on lipid-lowering medications had achieved proper lipid control. Less than half of all patients were taking antihypertensive medications. The recommendation for

health care providers is to recall that treatment of these patients does not end with the coronary bypass, since patients with cardiovascular disease often fail to make lifestyle changes. Each encounter with these patients during follow-up after coronary bypass surgery should be utilized to assess what patients know about further reductions in cardiovascular risk factors and their progress toward lifestyle change.

Allen JK, Blumenthal RS, Margolis S, and Young DR: Status of secondary prevention in patients undergoing coronary revascularization. The American Journal of Cardiology 87: 1203-1206, 2001.

Reducing Incontinence Among People at Home with Dementia. Functional incontinence (FI) affects many memory-impaired elders and adds a burden to their caregivers. Nurse researchers examined the effectiveness of an individualized scheduled toileting (IST) program on reducing functional urinary incontinence in memory-impaired elders. A nurse practitioner worked with the patient's caregiver to design the IST. Monthly phone calls helped monitor compliance and address problems. At 6 months, 63 percent of patients in the IST group showed a decrease in incontinence episodes. The IST was most effective in patients with minimal impairment, and may help establish a routine as impairment worsens. Management of incontinence improves the quality of life of caregivers and patients with dementia, and may delay institutionalization.

Jirovec MM, and Templin T: Predicting success using individualized scheduled toileting for memory-impaired elders at home. Research in Nursing and Health 24: 1-8, 2001.

Advance Directives Help Lower Stress Levels in End-of-Life Decisions. Nurse investigators interviewed family members and clinicians after participation in a decision to withdraw support from a critically ill patient. Stress levels for family members were extremely high shortly after the event, and remained elevated even after 6 months. Highest stress levels were recorded in the absence of a patient advance directive. Both clinicians and family members cited patient preference as the chief factor in the decision. Advance directives can aid family members to reduce stress in end-of-life decisions.

Tilden VP, Tolle SW, Nelson CA, and Fields J: Family decision-making to withdraw life-sustaining treatments from hospitalized patients. Nursing Research 50: 105-115, 2001.

Reducing Cardiovascular Risk in Overweight Older Women. Researchers studied the effects of a diet and walking exercise intervention on obese, post-menopausal women. The women received instruction on maintaining a reduced-calorie, balanced diet. Also, they completed weekly treadmill sessions, and were instructed to walk at least two other days per week. After 6 months, body weight had decreased an average of 8 percent, aerobic capacity had increased 8 percent, and 25 percent fewer had impaired glucose tolerance. Improved fitness and decreased weight can reduce cardiovascular risk factors in obese older women.

Ryan AS, Nicklas BJ, Berman DM, and Dennis KE: Dietary restriction and walking reduce fat deposition in the midthigh in obese older women. American Journal of Clinical Nutrition 72: 708-713, 2000.

Effect of School-Based Programs on Suicide Prevention. Nurse researchers examined three interventions for youth suicide prevention: Counselors CARE (C-CARE), a one-time assessment and coping session; C-CARE with Coping and Support Training (CAST), a twelve-session life-skills program; or the standard school assessment and monitoring treatment. All three groups reduced suicide risk behaviors. Both C-CARE groups showed enhanced self-esteem and family integration, and a decrease in depression. The C-CARE with CAST group showed further improvement in personal control, problem-solving, and family support. School-based suicide intervention programs can be effective and cost-efficient.

Randell BP, Eggert LL, and Pike KC: Immediate post intervention effects of two brief youth suicide prevention interventions. Suicide and Life-Threatening Behavior 31: 41-61, 2001.

Trends of Cigarette Use in Adolescents. Researchers in North Carolina surveyed middle school youths in three rural counties on smoking habits in relation to gender, ethnicity, self-esteem, physical activity, parental smoking, and socioeconomic status (SES). The rate of smoking was higher among Whites and Hispanics than among Black youths, and tended to increase in advanced grades and with lower SES. Low self-esteem was a risk factor for girls. They noted no overall correlation between smoking and gender, physical activity, or parental use.

Lewis PC, Harrell JS, Bradley C, and Deng S: Cigarette use in adolescents: the cardiovascular health in children and youth study. Research in Nursing and Health 24: 27-37, 2001.

Employment has Little Effect on High-Risk Pregnancy Outcomes. Researchers analyzed the employment patterns of high-risk pregnant women. Most of the employed women stopped work at some point following their high-risk diagnosis, most often for bed rest. However, this treatment had no effect on the rate of preterm delivery. Most of the employed women returned to work after delivery. Welfare reforms will likely increase the number of women working while pregnant. These data suggest that employment does not increase the risk of preterm delivery.

Youngblut JM, Madigan EA, Neff DF, Deoisres W, Siripul P, and Brooten D: Employment patterns and timing of birth in women with high-risk pregnancies. Journal of Obstetric, Gynecologic and Neonatal Nursing 29: 137-144, 2000.

Drug Ototoxicity. Audiologic monitoring guidelines have been established for patients at risk for ototoxicity from cancer chemoprevention agents and are now being utilized across the country for patients being treated with these agents.

Shotland LI, Ondrey FG, Mayo KA, and Viner JL: Recommendations for cancer prevention trials using potentially ototoxic test agents. Journal of Clinical Oncology 19: 1658-1663, 2001.